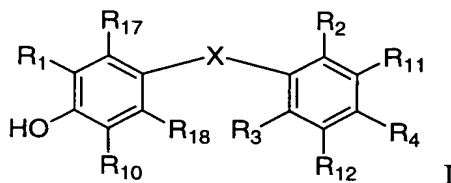


WHAT IS CLAIMED IS:

1. A compound of the formula

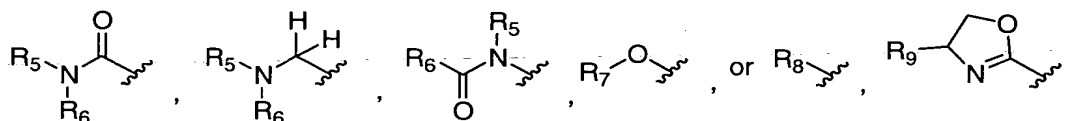
5



wherein

R1 is

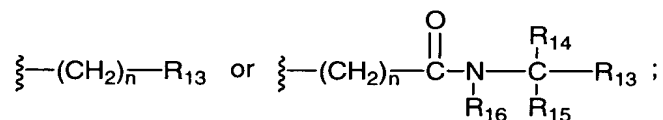
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R2 and R3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 5 carbons, provided that at least one of R2 and R3 is other than hydrogen;

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R4 is



R5 and R6 are the same or different and are selected from hydrogen, aryl, heteroaryl, alkyl, cycloalkyl, aralkyl or heteroaralkyl.

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R7 is aryl, heteroaryl, alkyl, aralkyl, or heteroaralkyl;

R8 is aryl, heteroaryl, or cycloalkyl;

R9 is R7 or hydrogen;

R10 is hydrogen, halogen, cyano or alkyl;

25 R11 and R12 are each independently selected from the group consisting of hydrogen, halogen, alkoxy, hydroxy, cyano, and alkyl;

R13 is carboxylic acid (COOH) or esters thereof, phosphonic and phosphinic acid or esters thereof, sulfonic acid, tetrazole, hydroxamic acid, thiazolidinedione, acylsulfonamide, or other carboxylic acid surrogates known in the art;

R14 and R15 may be the same or different and are selected from hydrogen and alkyl, or R14 and R15 may be joined together forming a chain of 2 to 5 methylene groups $[-(\text{CH}_2)_m-]$, $m = 2, 3, 4$ or 5 , thus forming 3- to 6-membered cycloalkyl rings;

R16 is hydrogen or alkyl of 1 to 4 carbons;

R17 and R18 are the same or different and selected from hydrogen, halogen and alkyl;

n is 0 or an integer from 1 to 4; and

X is oxygen (-O-), sulfur (-S-), sulfonyl ($-\text{SO}_2-$), sulfenyl ($-\text{SO}-$) selenium (-Se-), carbonyl ($-\text{CO}-$), amino ($-\text{NH}-$) or methylene ($-\text{CH}_2-$); and including all prodrugs, stereoisomers and pharmaceutically acceptable salts thereof.

2. A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

3. A pharmaceutical composition comprising a compound as defined in claim 2 and at least one additional therapeutic agent selected from the group consisting of other compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents, appetite suppressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

4. The pharmaceutical composition of claim 3 wherein said additional therapeutic agent is an antidiabetic agent selected from the group consisting of a biguanide, a glucosidase inhibitor, a meglitinide, a sulfonylurea, a thiazolidinedione, a PPAR-alpha agonist, a PPAR-gamma agonist, a PPAR alpha/gamma dual agonist, an SGLT2 inhibitor, a glycogen phosphorylase inhibitor, an αP2 inhibitor, a glucagon-like peptide-1 (GLP-1), a dipeptidyl peptidase IV inhibitor and insulin.

5 5. The pharmaceutical composition of claim 3 wherein said additional therapeutic agent is an antidiabetic agent selected from the group consisting of metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, troglitazone, pioglitazone, englitazone, darglitazone, rosiglitazone and insulin

10 6. The pharmaceutical composition of claim 3 wherein said additional therapeutic agent is an anti-obesity agent is selected from the group consisting of an aP2 inhibitor, a PPAR gamma antagonist, a PPAR delta agonist, a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin reuptake inhibitor, a cannabinoid-1 receptor antagonist and an anorectic agent.

15 7. The pharmaceutical composition of claim 3 wherein said additional therapeutic agent is a hypolipidemic agent selected from the group consisting of a thiazolidinedione, an MTP inhibitor, a squalene synthetase inhibitor, an HMG CoA reductase inhibitor, a fibric acid derivative, an ACAT inhibitor, a cholesterol absorption inhibitor, an ileal Na⁺/bile cotransporter inhibitor, a bile acid sequestrant and a nicotinic acid or a derivative thereof.

20 8. A method for preventing, inhibiting or treating a disease associated with metabolism dysfunction, or which is dependent on the expression of a T₃ regulated gene, which comprises administering to a mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

25 9. A method for treating or delaying the progression or onset of obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disorder or disease, which comprises
30 administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

10. The method according to claim 9 wherein the skin disorder or disease is dermal atrophy, post surgical bruising caused by laser resurfacing, keloids, stria, cellulite, roughened skin, actinic skin damage, lichen planus, ichthyosis, acne, psoriasis, Dernier's disease, eczema, atopic dermatitis, chloracne, pityriasis or skin
5 scarring.

11. The method according to claim 9 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from the group consisting of other compounds of
10 formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents, appetite suppressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

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12. A method of treating or delaying the progression or onset of a skin disorder or disease which comprises administering to a mammalian patient a therapeutically effective amount of a compound as defined in claim 1 in combination with a retinoid or a vitamin D analog.

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13. A method for treating or delaying the progression or onset of obesity which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

25 14. A method according to claim 13 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from the group consisting of an anti-obesity agent and an appetite suppressant.

30 15. A method according to claim 14 wherein said anti-obesity agent is selected from the group consisting of aP2 inhibitors, PPAR gamma antagonists, PPAR

delta agonists, beta 3 adrenergic agonists, lipase inhibitors, serotonin (and dopamine) reuptake inhibitors, other thyroid receptor agents and anorectic agents.

16. A pharmaceutical composition which functions as a selective agonist
5 of the thyroid hormone receptor-beta comprising a compound as defined in claim 1.